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## THE PATHOGENESIS OF HUMAN BLADDER CANCER

The specific aims of this project were to study the relationship between:

1. Detailed smoking, occupational, residential and family histories;
2. Levels of urinary excretion of urinary metabolites; and
3. The pathology and clinical course of patients with bladder cancer.

I will briefly discuss our progress with regard to each of these specific aims.

## Interview Studies

We have interviewed 141 patients with bladder cancer, 106 males and 35 females. A majority of interviews were patients originally treated at either the New England Deaconess or New England Baptist Hospitals, but recently we have begun to interview patients treated in the Boston Veteran's Administration Hospital as well. We are pleased at gaining access to this latter group of patients for we feel it represents a different population than we had previously been studying. For example, in 4 of the first 16 cases seen at the V. A. Hospital a history of employment in the rubber industry was found.

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We have interviewed 176 control subjects, 90 male and 86 female. The selection of an appropriate control population for such an interview study has been somewhat difficult, however, and we have enlisted the assistance of epidemiologists at the Harvard School of Public Health in making this selection. They have been of great help to us, but in addition, and perhaps of greater significance, I believe members of that department have become sufficiently interested in exploring the epidemiology of

bladder cancer to collaborate in a more extensive interview study. This study would cover the greater Boston area and should more accurately reflect the possible influence of environmental factors in the pathogenesis of this disease.

Thus far 34% of the females and 75% of the male bladder cancer patients who have been interviewed have smoked. This is approximately the same ratio as in our control population, but at present we are attaching no significance to these figures. No significant trend is yet apparent in our data concerning occupational or residential history but 48% of the female and 48% of the male population with bladder cancer have a family history of cancer. Again I am reluctant to comment about the significance of these numbers until we have reviewed our data with our statistical consultants.

By the end of the period covered in this report we had obtained the services of a second trained interviewer and with the additional funds furnished by The Council For Tobacco Research-USA we had obtained the part-time services of Dr. Carl Cornil, a trained urologist.

#### Tryptophan Metabolites

With regard to tryptophan metabolite excretion we have carried out 24, 48 or 96 hour studies on 63 patients and 32 controls. Not all of the urine samples have been assayed but thus far it would appear that approximately one third of the patients with bladder tumors have abnormal excretion of tryptophan metabolites. If one excludes patients with papillomas from the group of tumor cases, approximately one half of the remaining patients have abnormal values. This latter figure is similar to the one originally published by Price and his co-workers for the 41 Madison patients with bladder tumors.

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In our material it would appear that the histological grade and extent of the tumors are related to abnormal urinary metabolite concentrations. A review of the original pathological material from Dr. Price's group of 41 cases suggests that in

this group also the extent of the tumor was related to the presence or absence of abnormal urinary metabolite values. This review was conducted by Dr. Safouh Atassi and me in Madison within the past few months.

#### Pathology and Clinical Course

Dr. Spencer Burney and I, in Boston, have almost completed our review of the pathology from all of the bladder tumor patients whom we have thus far interviewed. In addition we are almost through with a review of 25 cases in which giant histologic sections were prepared. These latter studies should be suitable for publication within the next few months.

A great deal of time and energy has been spent following up the histories of all patients treated for bladder cancer at the New England Deaconess and New England Baptist Hospitals. From this review the fact has emerged that the majority of patients surviving their primary therapy will be found in the first 5 years after treatment. We will shortly have fairly complete information about 5, 10 and 15 year survival in bladder cancer patients treated at these two institutions. Such information has heretofore not been available.

#### Financial Support

Finally, it should be noted that we have been awarded a research grant from the U. S. Public Health Service to continue our bladder cancer studies for a 4 year period. This grant will supplement funds from The Council For Tobacco Research-USA for the first 2 years and then will furnish entire support for the last 2 years of our proposed research project. The grant year for the Public Health Service award began April 1, 1967. The sums awarded for each of the 4 grant years are \$31,307.00, \$46,935.00, \$57,185.00, and \$13,761.00.

At this time we hope that The Council For Tobacco Research-USA will see fit to renew its award to us for a second year beginning November 1, 1967. We do not anticipate asking The Council for additional support for this project beyond the second grant year.

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